## NON-TECHNICAL ABSTRACT

Cancer is the second leading cause of deaths in the United States. The majority of cancer deaths result from the dissemination of cancer cells from their original site to other organs in the body. Except for a few uncommon cancers, disseminated cancer is not curable, and currently available treatment provide at best slight prolongation of life. Recent advances in basic science research has enabled the development of new strategies in fighting disseminated cancers. For instance, tumor cells can be altered so that they become susceptible to drugs which would otherwise have no effect. Alternatively, tumor cells can be altered so that they are more effective in producing immunity in the patient, which in turn can kill other tumor cells. These alterations are accomplished by inserting a gene into the tumor cell with the help of a virus which has also been previously cahnged such that it does not reproduce and produce infection.

Mammalian cells are resistant to a drug called ganciclovir. However, if these cells are altered by inserting a gene called Herpes simplex thymidine kinase gene with the help of adenovirus (ADV-tk), these cells are killed by ganciclovir. Moreover, it is not necessary to alter all the cells in a tumor; only a small proportion needs to be altered for the tumor to be killed with ganciclovir. The thymidine kinase gene, which is derived from the Herpes simplex virus, produces an enzyme which causes ganciclovir to kill the cells which produces the enzyme. Adenovirus is a common virus which produces the symptoms of the common cold.

Studies in mice have shown that if ADV-tk is directly injected into tumors with a thin needle and ganciclovir admdinistered afterwards, these tumors are killed. An intense inflammatory reaction is seen at the site of these dying tumors, indicating that an immune reaction has been produced which can continue to kill other tumor cells. These animal studies also showed that the injections and ganciclovir are safely tolerated.

The current study in patients with disseminated cancers aims to see if these cancers can be treated safely and effectively by injecting ADV-tk directly into a tumor in the liver with a thin needle, followed by administration in the vein of ganciclovir twice a day for seven days. Each patient will receive one injection of ADV-tk only. The starting dose of ADV-tk is chosen because it has been shown to be safely tolerated in mice. The ADV-tk dose will then be gradually increased in subsequent patients if no serious side effects are observed. Patients are also tested for shrinkage in the size of their tumors and for signs of an immune reaction in the tumors and in the blood.

ADV-tk has been previously approved by the National Institute of Health and the Food and Drugs Administration for studies of direct injection into the tumors of patients with brain, head and neck, and prostate cancers. The prostate cancer trial is currently ongoing. The preparation of ADV-tk used in this study will be obtained from the same preparation used in prostate cancer which has been tested and approved by the Food and Drugs Administration.